The Effect of Hyperprolactinemia on Semen Parameters

Hiperprolaktineminin Semen Parametreleri Üzerine Etkisi

Hyperprolactinemia and Spermiogram

Mehmet Zeynel Keskin[1], Salih Budak[1], Saim Gubari[2], Orcun Celik[1], Okan Nabi Yalbuzdağ[1], Yusuf Özlem İlbey[1]
[1] Urology Clinic, [2]Clinical Embryology, Aegean Maternity Hospital ART Center, Tepecik Training and Research Hospital, Izmir, Turkey

Özet

Amaç: Hiperprolaktineminin semen parametrelerine olumsuz etkileri bilinmektedir, ancak bu etki açık değildir. Bu çalışmamızda, hiperprolaktineminin semen parametrelerine etkilerini değerlendirmeyi amaçladık. Gereç ve Yöntem: Çalışmamıza hastanemiz erkek infertilitesi polikliniğine başvuran 334 hasta dahil edildi. Hastaların prolaktin düzeyi ve semen analizi çalışıldı. Prolaktin için sınır değer 20 ng/ml, sperm konsantrasyonu için 15x10^6/ml, total motilite için %40, ileri motilite için %32, morfoloji için %4 kabul edildi. Bulgular: Hastaların ortalama prolaktin, sperm konsantrasyonu, total motilite, ileri motilite değerleri sırasıyla 11,07 ng/ml, 26x106/ml, %42, %29'du. Prolaktin düzeyleri ile semen parametrelerinin hiç birinde istatistiksel olarak anlamlı derecede ilişki bulunmadı. Tartışma: Prolaktin düzeyi ile semen parametreleri arasında anlamlı ilişki saptanmamış olsa da literatürdeki veriler ışığında sperm konsantrasyonu 10x10^6/ml'nin altında olan hastalarda prolaktin seviyesinin çalışılmasını önermekteyiz.

Anahtar Kelimeler

İnfertilite; Prolaktin; Semen Parametreleri; Spermiyogram

Abstract

Aim: Hyperprolactinemia is known adverse effects on semen parameters but this effect is not clear. In this study, we aimed to evaluate the effects of hyperprolactinemia on semen parameters. Material and Method: The study comprised 334 patients who presented to the outpatient clinics for male infertility. Prolactin levels were measured and semen analysis was performed on all patients. The limit values for prolactin, sperm concentration and total motility, progressive motility, and morphology were determined to be 20 ng/ml, 15x10^6/ml, 40%, 32%, and 4%, respectively. Results: Levels of mean prolactin, sperm concentration, total mortality, progressive motility values were 11.07 ng/ml, 26x10^6/ml, 42%, and 29%. No significant differences were found in any of the semen parameters according to the prolactin levels (p>0.05). Discussion: Although no significant association between the prolactin level and semen parameters was detected, we suggest that prolactin levels should be tested in patients with a sperm concentration of less than 10x10^6/ml in light of literature data.

Keywords

Infertility; Prolactin; Semen Parameters; Spermiogram

DOI: 10.4328/JCAM.3186 Received: 29.12.2014 Accepted: 18.01.2015 Printed: 01.11.2016 J Clin Anal Med 2016;7(6): 757-9
Corresponding Author: Mehmet Zeynel Keskin, Tepecik Training and Research Hospital, Urology Clinic, Izmir, Turkey.
GSM: +905422503256 F.: +90 2324330756 E-Mail : zeynel_akd@hotmail.com

Introduction

Prolactin synthetized in the anterior lobe of the hypophysis gland is a hormone that has an effect on sexual and metabolic functions in the polypeptide structure [1]. Prolactin stimulates testicular function in men [2]. Although the role of prolactin in men is not clearly understood, it is suggested to maintain the intratesticular testosterone (T) levels by increasing the luteinizing hormone (LH) receptors in Leydig cells [3]. Hyperprolactinemia is the cause of oligospermia in 11% of the cases [4]. Prolactin decreases the levels of follicle stimulating hormone (FSH), LH, and T by inhibiting the pulsatile release of gonadotropin releasing hormone (GNRH) [4]. Finally, it causes an interruption of spermatogenesis and impairment of the sperm quality and motility [4]. A normal level of serum prolactin is less than 20 ng/ml [5, 6]. The prolactin levels in our study are mild or moderate and it is not clear that in which level of prolactin adversely affect semen parameters. Especially mild or moderate serum prolactin levels have an uncertain effects in the impact of semen parameters. In this study, we aimed to determine the effects of prolactin levels on semen parameters in 334 patients who presented to our infertility center.

Material and Method

Three hundred thirty-four patients presented to the outpatient clinics of urology for infertility at the Tepecik education and research hospital between July and October 2014 were included in the study. Prolactin level and spermiogram analysis were ordered during the first visit to the clinic. A second analysis was not ordered in patients whose spermiogram analysis was found to be normal; on the other hand, a second analysis was ordered in patients with abnormalities in the first test. Each analysis was performed following refraining sex for 3-6 days and the waiting period between the two tests was at least 15 days, when performed. Spermiograms were evaluated by the same embryologist at the spermiogram laboratory of this in vitro fertilization center.

The evaluation was performed according to the WHO 2010 criteria (semen volume ≥ 1.5ml, sperm concentration ≥ 15 × 10^6 / ml; total motility ≥ 40%, progressive motility ≥ 32% and morphology ≥ 4%) [7]. Blood samples for determination of hormone levels were collected before 10:00 am. Hormone analysis was performed with a Roche Cobas e 601 HITACHI device by microparticle enzyme immunoassay. Reference values for prolactin were determined to be 20 ng/ml. Cabergoline treatment was initiated when the prolactin level was higher than 50 ng/ml and hypophyseal MRI was planned to be ordered when the prolactin value was higher than 150 ng/ml.

Statistical associations between hyperprolactinemia and semen parameters were evaluated using the IBM Statistical Package for Social Sciences (SPSS) Version 22.0 program. p value < 0.05 was accepted as significant.

Results

Mean prolactin level and sperm concentration and mean total motility and advanced motility were found to be 11.07 ± 6 ng/ml, 26x10^6, 42%, and 29%, respectively among the 334 patients who were included in the study (Table I).

The patients were divided into two groups according to their prolactin levels. Patients with a prolactin level of 0-20 ng/ml comprised Group 1 (n=285) and patients with a prolactin level of ≥20 ng/ml comprised Group 2 (n=49) (Table II). Patients were divided into five groups according to their sperm concentration: patients with sperm concentration >15x10^6, Group 1 (n=160), 5x10^6-15x10^6, Group 2 (n=42), 1x10^6-5x10^6, Group 3 (n=49), < 1x10^6 group 4 (n=20), azoospermia and cryptozoospermia, Group 5 (n=63) (Table III). No statistically significant differences were found between the prolactin levels according to the sperm concentration (p> 0.05).

Table I. Mean data of patients

	N	Min.	Max.	Mean	Std. Dev.
PROLACTIN	334	1.32	70.56	11.07	6.06
CONCENTRATION	334	0.00	190.00	26.98	34.08
TOTAL MOTILITY	334	0.00	90.00	42.42	26.69
PROG. MOTILITY	334	0.00	80.00	29.25	22.11

Table II. Distribution of cases according to the prolactin levels

Group	Number(n)	Percentage (%)
1 (<20ng/ml)	285	85.3
2 (≥20ng/ml)	49	14.7
Total	334	100.0

Table III. Prolactin levels in different sperm concentration levels

	Prolactin Level				
Sperm Concentration Group	N	Mean	Std. Dev.	Min.	Max.
≥15x106 (Group 1)	160	11.20	6.86	1.32	70.56
5x106-15x106 (Group 2)	42	10.34	6.01	3.52	36.20
1x106-5x106 (Group 3)	49	10.63	5.54	1.63	27.71
< 1x106 (Group 4)	20	12.13	4.84	5.00	22.00
Azoospermia/Cryptozoospermia (Group 5)	63	11.25	4.58	3.86	26.70
Total	334	11.07	6.06	1.32	70.56

According to the limit value of total motility as 40%, the total motility was less than 40% in 114 patients (Group 1) and was higher than 40% in 220 patients (Group 2) (Table IV). Prolactin levels and percentages of total motility were not found to be statistically associated (Pearson Chi-Square, p>0.05). According to the limit value of progressive motility as 32%, the progressive motility was less than 32% in 180 patients (Group 1) and was higher than 32% in 154 patients (Group 2) (Table V). Prolactin levels and percentages of progressive motility were not found to be statistically associated (Pearson Chi-Square, p>0.05). According to the limit value of morphology as 4%, this value was less than 4% in 271 patients (Group 1) and was high-

Table IV. Comparison of prolactin levels and percentages of total motility

	Total Motility group		
Prolactin group	1 (< 40%)	2 (≥ 40%)	Total
1 (<20ng/ml)	103	182	285
2 (≥20ng/ml)	11	38	49
Total	114	220	334

Table V. Comparison of prolactin levels and percentages of progressive motility

	Progressive group	Motility	
Prolactin group	1 (< %32)	2 (≥ %32)	Total
1 (<20ng/ml)	158	127	285
2 (≥20ng/ml)	22	27	49
Total	180	154	334

er than 4% in 63 patients (Group 2) (Table VI). Prolactin levels and percentages of morphology were not found to be statistically associated (Pearson Chi-Square, p>0.05).

Table VI. Comparison of prolactin levels and percentages of morphology

	Morphology group		
Prolactin group	1 (< %4)	2 (≥ %4)	Total
1 (< 20ng/ml)	231	54	285
2 (≥ 20ng/ml)	40	9	49
Total	271	63	334

Discussion

Prolactin increases the production of steroids and androgen by increasing the LH receptors in Leydig cells, increases FSH receptors in Sertoli cells, and increases the total lipid production in germ cells and conversion of spermatocyte to spermatid [8]. In hyperprolactinemia, serum T levels are generally low without an accompanying increase in LH levels and this suggests that there is no role of the hypothalamo-hypophyseal axis on the increased levels of prolactin [3].

Among the studies on the effects of prolactin on semen parameters, some of them reported existence of an association among these two parameters [4, 9-15], while no association was found between the two in some other studies [16]. No statistically significant association was found between prolactin level and semen parameters in this present study. However, studies suggesting an association between these two parameters predominate in the literature. Limit values may be different among various laboratories for prolactin levels. A limit value of 20 ng/ml was defined in our study. Comorbid diseases were not found in patients with hyperprolactinemia.

In a study by Alici et al. [17] that was published in 1998, an association between hyperprolactinemia and semen parameters was analyzed with a defined limit value of prolactin as 10ng/ml in 1,465 patients. They found hyperprolactinemia in 85 out of 1,465 patients and detected slight association between all semen parameters and prolactin levels. In addition, they found that treatment of hyperprolactinemia had no effect on prolactin levels.

In a study by Al-Daghistani et al. [18] in 2006, 120 patients presented with the complaint of infertility were divided into four groups of asthenozoospermia, oligozoospermia, severe oligozoospermia, and azoospermia. They analyzed the relation of prolactin and gonadotropin levels with different sperm concentrations and found that the prolactin level had an effect on sperm concentration and motility, FSH level had a statistical effect on motility in especially azoospermic patients, and that LH level had no statistical effect on motility. They found that prolactin level was a more effective parameter compared to the FSH level on the level of concentration [18]. In a Review by Vandekerckhove et al, includes four studies, had reported that bromocriptine reduces prolactin levels in subfertile men with normal gonadotrophins and treatment of hyperprolactinemia has no effect on semen parameters [19]. As shown, there are contradictory findings in the previous studies and prolactin limit value for infertility is not determined precisely. Hence, it seems that this issue will employ the journal occasionally. Although a significant association between prolactin level and semen parameters was not found as a result of the analysis of our data, we recommend that prolactin levels should be tested in patients with a sperm concentration of less than $10x10^6$/ml according to the literature findings.

Competing interests

The authors declare that they have no competing interests.

References

1. Bolyakov A, Paduch DA. Prolactin in men's health and disease. Curr Opin Urol 2011;21(6):527-34.
2. Buntin JD, Tesch D. Effects of intracranial prolactin administration on maintenance of incubation readiness, ingestive behavior, and gonadal condition in ring doves. Horm Behav 1985;19(2):188-203.
3. Alan J. Wein, MD, PhD (Hon), FACS Louis R. Kavoussi, MD, MBA Andrew C. Novick, MD, Alan W. Partin, MD, PhD and Craig A. Peters, MD, FACS, FAAP. Campbell-Walsh Urology. 10th ed. Philadelphia: 2014. Chapter 21.
4. Masud S, Mehboob F, Bappi MU. Severe hyperprolactinemia directly depresses the gonadal activity causing infertility. Esculapio J Services Inst Med Sci 2007;2:25-7.
5. Casanueva FF, Molitch ME, Schlechte JA, Abs R, Bonert V, Bronstein MD, et al. Guidelines of the Pituitary Society for the diagnosis and management of prolactinomas. Clin Endocrinol (Oxf) 2006;2:265-73.
6. Aşçı R, Çayan S, Erdemir F, Orhan İ, Yaman Ö, Usta MF, et al. Erkek Üreme Sistemi Hastalıkları ve Tedavisi. 1. Baskı. İstanbul: 2013.s.693-8.
7. World Health Organization. WHO Laboratory Manual for the Examination and Processing of Human Semen. 5th ed. WHO. 2010.
8. Gunasekar PG, Kumaran B, Govindarajulu P. Role of prolactin on Leydig, Sertoli and germ cellular neutral lipids in bonnet monkeys, Macaca radiata. Endocrinol Jpn 1991;38(1):1-8.
9. Segal S, Polishuk WZ, Ben-David M. Hyperprolactinemic male infertility. Fertil Steril 1976; 27(12):1425-7.
10. Smith ML, Luqman WA, Rakoff JS. Correlations between seminal radioimmunoreactive prolactin, sperm count, and sperm motility in prevasectomy and infertility clinic patients. Fertil Steril 1979;32(3):312-5.
11. Buvat J. Hyperprolactinemia and sexual function in men: a short review. Int J Impot Res 2003;15:373-7.
12. De Rosa M, Zarrilli S, Di Sarno A, Milano N, Gaccione M., Boggia B, et al. Hyperprolactinemia in men. Endocrine 2003;20(1-2):75-82.
13. Soler FJ, Caravaca MF, Domínguez BC, Murillo MJ, Aparicio PA, Herrera PJ. Correlation of serum prolactin, sperm count and motility. Prevalence of hyperprolactinemia in the infertile male. Arch Esp Urol 1990;43(8):891-5.
14. Laufer N, Yaffe H, Margalioth EJ, Livshin J, Ben-David M, Schenker JG. Effect of bromocriptine treatment on male infertility associated with hyperprolactinemia. Syst Biol Reprod Med 1981;6(4):343-6.
15. Singh P, Singh M, Cugati G, Singh AK. Hyperprolactinemia: An often missed cause of male infertility. J Hum Reprod Sci 2011;4(2):102.
16. Eggert-Kruse W, Schwalbach B, Gerhard I, Tilgen W, Runnebaum B. Influence of serum prolactin on semen characteristics and sperm function. Int J Fertil 1991;36(4):243.
17. Alıcı B, Çitçi A, Özkara H, Akkuş E, Hattat H. The effect of the hyperprolactinemia on semen parameters in male infertility. Cerrahpaşa J Med 1998;29 (2):95-8.
18. Al-Daghistani H, Abdel-Dayem M. Hyperprolactinemia and hypergonadotropins in infertile males with Severe oligospermia and azoospermia. The Internet J Endocrinol 2002;3(1):1540-2606.
19. Vandekerckhove P, Lilford R, Vail A, Hughes E. Bromocriptine for idiopathic oligo/asthenospermia. Cochrane Database Syst Rev 2000;(2):CD000152. Review. Update in: Cochrane Database Syst Rev 1996;(4):CD000152.

How to cite this article:
Keskin MZ, Budak S, Gubari S, Celik O, Yalbuzdağ ON, İlbey YÖ. The Effect of Hyperprolactinemia on Semen Parameters. J Clin Anal Med 2016;7(6): 757-9.